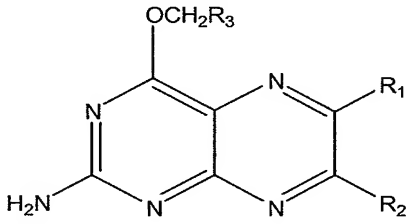
AMENDMENTS TO THE CLAIMS

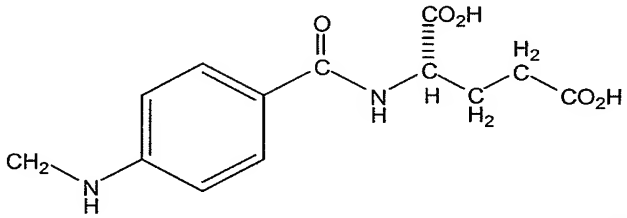
This listing of claims replaces all prior versions, and listings, of claims in the application.

1. (Currently Amended) A compound of formula (I):



(I)

wherein R_1 and R_2 are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, carboxyl, formyl, C_1-C_6 hydroxyalkyl, C_1-C_6 carboxyalkyl, C_1-C_6 formyl alkyl, C_1-C_6 alkoxy, acyloxy, acyloxy C_1-C_6 alkyl, halo, hydroxy, aryl, amino, monoalkylamino wherein the alkyl is C_1-C_6, dialkylamino wherein the alkyl is C_1-C_6, acylamino, C_1-C_6 alkyl substituted aryl, nitro, C_3-C_8 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, and a group of formula (II):



(II);

R_3 is (a) phenyl; (b) a cyclic group having at least one 5 or 6-membered heterocyclic ring, optionally with a carbocyclic or heterocyclic ring fused thereto, wherein each heterocyclic ring has at least one hetero atom chosen from O, N, or S; or (c) a phenyl group or a cyclic group, said cyclic group optionally with a carbocyclic or heterocyclic ring fused thereto, which is substituted with 1 to 5 substituents selected from the group consisting of halogen, hydroxy, aryl, C_1-C_6 alkyl substituted aryl, nitro, polycyclic aryl alkyl containing 2 to 4 aromatic rings wherein the alkyl is a C_1-C_6, C_3-C_8 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 hydroxyalkyl, C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl, aryloxy, acyloxy, acyloxy C_1-C_6 alkyl, amino, monoalkylamino wherein the alkyl is C_1-C_6, dialkylamino wherein the alkyl is C_1-C_6, acylamino, ureido, thioureido, carboxy, carboxy C_1-C_6 alkyl, azido, cyano,

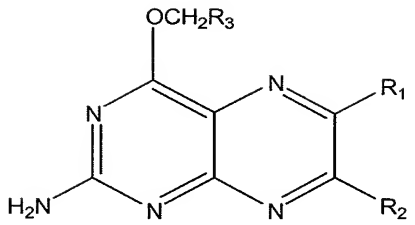
cyano C_1-C_6 alkyl, formyl, acyl, dialkoxy alkyl wherein the alkoxy and alkyl are independently C_1-C_6, aminoalkyl wherein the alkyl is C_1-C_6, and SO_nR' wherein n=0, 1, 2 or 3, R' is H, a C_1-C_6 alkyl or aryl;
or a pharmaceutically acceptable salt thereof;
with the provisos that (1) R_1 and R_2 are not simultaneously hydrogen; [[and]] (2) when R_3 is unsubstituted phenyl, R_1 and R_2 are not simultaneously ~~methyl.~~ methyl; and (3) when R_1 or R_2 is alkyl, R_3 is not a phenyl group substituted with a halogen or a cyclic group having at least one 5-membered heterocyclic ring substituted with a halogen.

2. (Original) The compound of claim 1, wherein R_3 is phenyl or a phenyl group substituted with 1 to 5 substituents selected from the group consisting of halo, hydroxy, aryl, C_1-C_6 alkyl substituted aryl, nitro, polycyclic aryl alkyl containing 2 to 4 aromatic rings wherein the alkyl is a C_1-C_6, C_3-C_8 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 hydroxyalkyl, C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl, aryloxy, acyloxy, acyloxy C_1-C_6 alkyl, amino, monoalkylamino wherein the alkyl is C_1-C_6, dialkylamino wherein the alkyl is C_1-C_6, acylamino, ureido, thioureido, carboxy, carboxy C_1-C_6 alkyl, azido, cyano, cyano C_1-C_6 alkyl, formyl, acyl, dialkoxy alkyl wherein the alkoxy and alkyl are independently C_1-C_6, aminoalkyl wherein the alkyl is C_1-C_6, and SO_nR' wherein n=0, 1, 2 or 3, R' is H, a C_1-C_6 alkyl or aryl; or a pharmaceutically acceptable salt thereof.

3. (Original) The compound of claim 2, wherein R_1 is selected from the group consisting of hydrogen, C_1-C_6 alkyl, carboxyl, formyl, C_1-C_6 hydroxyalkyl, C_1-C_6 carboxyalkyl, C_1-C_6 formyl alkyl, and a group of formula (II) and R_2 is hydrogen or C_1-C_6 alkyl; and R_3 is phenyl; or a pharmaceutically acceptable salt thereof.

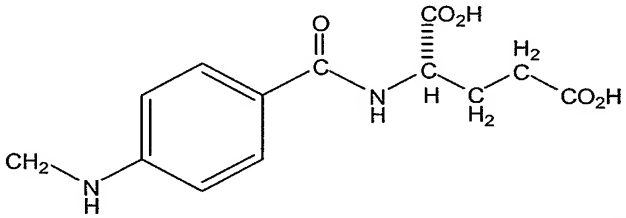
4. (Original) The compound of claim 3, wherein R_1 is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, carboxyl, formyl, and a group of formula (II) and R_2 is hydrogen or C_1-C_6 alkyl; or a pharmaceutically acceptable salt thereof.

5. (Currently Amended) ~~The compound of claim 4,~~ A compound of formula (I):



(I)

wherein R_1 is hydroxymethyl, carboxyl, formyl, or a group of formula (II), [[and]] R_2 is hydrogen;



(II);

and R_3 is phenyl or a phenyl group substituted with 1 to 5 substituents selected from the group consisting of halo, hydroxy, aryl, C_1-C_6 alkyl substituted aryl, nitro, polycyclic aryl alkyl containing 2 to 4 aromatic rings wherein the alkyl is a C_1-C_6, C_3-C_8 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 hydroxyalkyl, C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl, aryloxy, acyloxy, acyloxy C_1-C_6 alkyl, amino, monoalkylamino wherein the alkyl is C_1-C_6, dialkylamino wherein the alkyl is C_1-C_6, acylamino, ureido, thioureido, carboxy, carboxy C_1-C_6 alkyl, azido, cyano, cyano C_1-C_6 alkyl, formyl, acyl, dialkoxy alkyl wherein the alkoxy and alkyl are independently C_1-C_6, aminoalkyl wherein the alkyl is C_1-C_6, and SO_nR' wherein n=0, 1, 2 or 3, R' is H, a C_1-C_6 alkyl or aryl;

or a pharmaceutically acceptable salt thereof.

6. (Original) The compound of claim 5, wherein R_1 is hydroxymethyl; or a pharmaceutically acceptable salt thereof.

7. (Original) The compound of claim 5, wherein R_1 is carboxyl; or a pharmaceutically acceptable salt thereof.

8. (Original) The compound of claim 5, wherein R_1 is formyl; or a pharmaceutically acceptable salt thereof.

9. (Original) The compound of claim 5, wherein R_1 is a group of formula (II); or a pharmaceutically acceptable salt thereof.

10. (Currently Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound or a pharmaceutically acceptable salt of claim 1.

11. (Original) The pharmaceutical composition of claim 10, further including an antineoplastic alkylating agent.

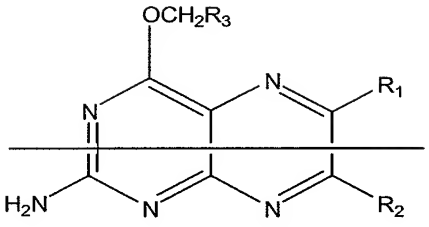
12. (Previously Presented) The pharmaceutical composition of claim 10, wherein the pharmaceutically acceptable carrier is polyethylene glycol.

13. (Previously Presented) The pharmaceutical composition of claim 11, wherein the antineoplastic alkylating agent is a chloroethylating agent.

14. (Previously Presented) The pharmaceutical composition of claim 11, wherein the antineoplastic alkylating agent is a methylating agent.

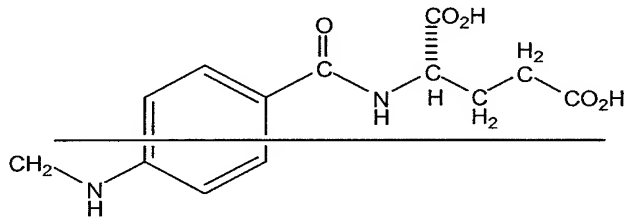
15. (Previously Presented) The pharmaceutical composition of claim 11, wherein the antineoplastic alkylating agent is selected from the group consisting of lomustine, carmustine, semustine, nimustine, fotomustine, mitozolomide, clomesone, temozolomide, dacarbazine, procarbazine, streptzocin, and combinations thereof.

16. (Withdrawn - Currently Amended) A method of enhancing the chemotherapeutic treatment of tumor cells in a mammal with an antineoplastic alkylating agent that causes cytotoxic lesions at the O^6 -position of guanine, which method comprises administering to the mammal an effective amount of a compound or a pharmaceutically acceptable salt of claim 1 ~~of formula (I):~~



~~(I);~~

~~wherein R_1 and R_2 are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, carboxyl, formyl, C_1-C_6 hydroxyalkyl, C_1-C_6 carboxyalkyl, C_1-C_6 formyl alkyl, C_1-C_6 alkoxy, acyloxy, acyloxy C_1-C_6 alkyl, halo, hydroxy, aryl, amino, monoalkylamino wherein the alkyl is C_1-C_6, dialkylamino wherein the alkyl is C_1-C_6, acylamino, C_1-C_6 alkyl substituted aryl, nitro, C_3-C_8 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl and a group of formula (II):~~



~~(II);~~

~~R_3 is (a) phenyl; (b) a cyclic group having at least one 5 or 6 membered heterocyclic ring, optionally with a carbocyclic or heterocyclic ring fused thereto, wherein each heterocyclic ring has at least one hetero atom chosen from O, N, or S; or (c) a phenyl group or a cyclic group, said cyclic group optionally with a carbocyclic or heterocyclic ring fused thereto, which is substituted with 1 to 5 substituents selected from the group consisting of halo, hydroxy, aryl, C_1-C_6 alkyl substituted aryl, nitro, polycyclic aryl alkyl containing 2 to 4 aromatic rings wherein the alkyl is a C_1-C_6, C_3-C_8 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 hydroxyalkyl, C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl, aryloxy, acyloxy, acyloxy C_1-C_6 alkyl, amino, monoalkylamino wherein the alkyl is C_1-C_6, dialkylamino wherein the alkyl is C_1-C_6, acylamino, ureido, thioureido, carboxy, carboxy C_1-C_6 alkyl, azido, cyano, cyano C_1-C_6 alkyl, formyl, acyl, dialkoxy alkyl wherein the alkoxy and alkyl are independently C_1-C_6, aminoalkyl wherein the alkyl is C_1-C_6, and SO_nR' wherein n=0, 1, 2 or 3, R' is H, a C_1-C_6 alkyl or aryl;~~

~~or a pharmaceutically acceptable salt thereof;~~

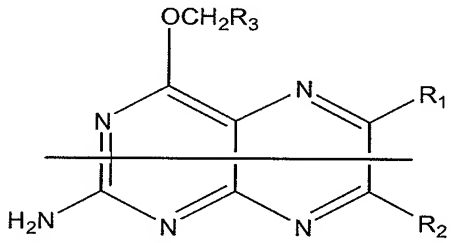
~~with the proviso that R_1 and R_2 are not simultaneously hydrogen;~~

and administering to the mammal an effective amount of an antineoplastic alkylating agent which causes cytotoxic lesions at the O^6-position of guanine.

17. (Withdrawn) The method of claim 16, wherein R_3 is phenyl or a phenyl group substituted with 1 to 5 substituents selected from the group consisting of halo, hydroxy, aryl, C_1-C_6 alkyl substituted aryl, nitro, polycyclic aryl alkyl containing 2 to 4 aromatic rings wherein the alkyl is a C_1-C_6, C_3-C_8 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 hydroxyalkyl, C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl, aryloxy, acyloxy, acyloxy C_1-C_6 alkyl, amino, monoalkylamino wherein the alkyl is C_1-C_6, dialkylamino wherein the alkyl is C_1-C_6, acylamino, ureido, thioureido, carboxy, carboxy C_1-C_6 alkyl, azido, cyano, cyano C_1-C_6 alkyl, formyl, acyl, dialkoxy alkyl wherein the alkoxy and alkyl are independently C_1-C_6, aminoalkyl wherein the alkyl is C_1-C_6, and SO_nR' wherein n=0, 1, 2 or 3, R' is H, a C_1-C_6 alkyl or aryl; or a pharmaceutically acceptable salt thereof.

18-30. (Canceled)

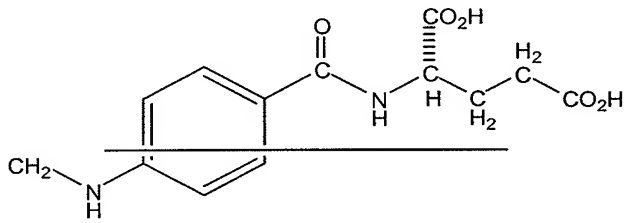
31. (Withdrawn - Currently Amended) A method for treating tumor cells in a mammal comprising administering to the mammal an amount effective to reduce the O^6-alkylguanine-DNA alkyltransferase activity in the mammal of a compound or a pharmaceutically acceptable salt of claim 1 ~~of formula (I):~~



~~(I);~~

~~wherein R_1 and R_2 are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, carboxyl, formyl, C_1-C_6 hydroxyalkyl, C_1-C_6 carboxyalkyl, C_1-C_6 formyl alkyl, C_1-C_6 alkoxy, acyloxy, acyloxy C_1-C_6 alkyl, halo, hydroxy, aryl, amino, monoalkylamino wherein the alkyl is C_1-C_6, dialkylamino wherein the alkyl is C_1-C_6, acylamino, C_1-C_6 alkyl~~

~~substituted aryl, nitro, C_3-C_8 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, and a group of formula (II):~~



~~(II);~~

~~R_3 is (a) phenyl or (b) a cyclic group having at least one 5 or 6 membered heterocyclic ring, optionally with a carbocyclic or heterocyclic ring fused thereto, wherein each heterocyclic ring has at least one hetero atom chosen from O, N, or S; or (c) a phenyl group or a cyclic group, said cyclic group optionally with a carbocyclic or heterocyclic ring fused thereto, which is substituted with 1 to 5 substituents selected from the group consisting of halogen, hydroxy, aryl, C_1-C_6 alkyl substituted aryl, nitro, polycyclic aryl alkyl containing 2 to 4 aromatic rings wherein the alkyl is a C_1-C_6, C_3-C_8 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 hydroxyalkyl, C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl, aryloxy, acyloxy, acyloxy C_1-C_6 alkyl, amino, monoalkylamino wherein the alkyl is C_1-C_6, dialkylamino wherein the alkyl is C_1-C_6, acylamino, ureido, thioureido, carboxy, carboxy C_1-C_6 alkyl, azido, cyano, cyano C_1-C_6 alkyl, formyl, acyl, dialkoxy alkyl wherein the alkoxy and alkyl are independently C_1-C_6, aminoalkyl wherein the alkyl is C_1-C_6, and SO_nR' wherein n=0, 1, 2 or 3, R' is H, a C_1-C_6 alkyl or aryl; or a pharmaceutically acceptable salt thereof;~~

~~with the proviso that R_1 and R_2 are not simultaneously hydrogen;~~

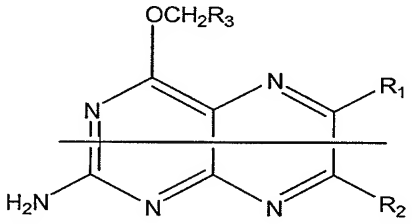
and administering to the mammal an effective amount of an antineoplastic alkylating agent which causes cytotoxic lesions at the O^6-position of guanine.

32. (Withdrawn) The method of claim 31, wherein R_3 is phenyl or a phenyl group substituted with 1 to 5 substituents selected from the group consisting of halo, hydroxy, aryl, C_1-C_6 alkyl substituted aryl, nitro, polycyclic aryl alkyl containing 2 to 4 aromatic rings wherein the alkyl is a C_1-C_6, C_3-C_8 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 hydroxyalkyl, C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl, aryloxy, acyloxy, acyloxy C_1-C_6 alkyl, amino, monoalkylamino wherein the alkyl is C_1-C_6, dialkylamino wherein the alkyl is C_1-C_6, acylamino, ureido, thioureido, carboxy, carboxy C_1-C_6 alkyl, azido, cyano, cyano

C_1-C_6 alkyl, formyl, acyl, dialkoxy alkyl wherein the alkoxy and alkyl are independently C_1-C_6, aminoalkyl wherein the alkyl is C_1-C_6, and SO_nR' wherein n=0, 1, 2 or 3, R' is H, a C_1-C_6 alkyl or aryl; or a pharmaceutically acceptable salt thereof.

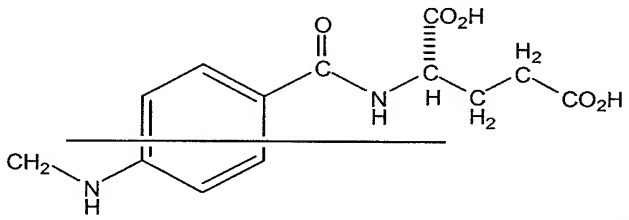
33-39. (Canceled)

40. (Withdrawn - Currently Amended) A method of inhibiting the reaction of O^6 -alkylguanine-DNA-alkyltransferase with an alkylated DNA comprising reacting the O^6 -alkylguanine-DNA-alkyltransferase with the compound of claim 1 ~~formula (I):~~



~~(I);~~

~~wherein R_1 and R_2 are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, carboxyl, formyl, C_1-C_6 hydroxyalkyl, C_1-C_6 carboxyalkyl, C_1-C_6 formyl alkyl, C_1-C_6 alkoxy, acyloxy, acyloxyalkyl wherein the alkyl is C_1-C_6, halo, hydroxy, aryl, amino, monoalkylamino wherein the alkyl is C_1-C_6, dialkylamino wherein the alkyl is C_1-C_6, acylamino, C_1-C_6 alkyl substituted aryl, nitro, C_3-C_8 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, and a group of formula (II):~~



~~(II);~~

~~R_3 is (a) phenyl or (b) a cyclic group having at least one 5 or 6 membered heterocyclic ring, optionally with a carbocyclic or heterocyclic ring fused thereto, wherein each heterocyclic ring has at least one hetero atom chosen from O, N, or S; or (c) a phenyl group or a cyclic group, said cyclic group optionally with a carbocyclic or heterocyclic ring fused thereto, which is substituted with 1 to 5 substituents selected from the group consisting of halogen,~~

~~hydroxy, aryl, C_1-C_6 alkyl substituted aryl, nitro, polycyclic aryl alkyl containing 2 to 4 aromatic rings wherein the alkyl is a C_1-C_6, C_3-C_8 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 hydroxyalkyl, C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl, aryloxy, acyloxy, acyloxy C_1-C_6 alkyl, amino, monoalkylamino wherein the alkyl is C_1-C_6, dialkylamino wherein the alkyl is C_1-C_6, acylamino, ureido, thioureido, carboxy, carboxy C_1-C_6 alkyl, azido, cyano, cyano C_1-C_6 alkyl, formyl, acyl, dialkoxy alkyl wherein the alkoxy and alkyl are independently C_1-C_6, aminoalkyl wherein the alkyl is C_1-C_6, and SO_nR' wherein n=0, 1, 2 or 3, R' is H, a C_1-C_6 alkyl or aryl;~~

or a pharmaceutically acceptable salt ~~thereof;~~

~~with the proviso that R_1 and R_2 are not simultaneously hydrogen;~~ thereof.

41. (Withdrawn) The method of claim 40, wherein R_3 is phenyl or a phenyl group substituted with 1 to 5 substituents selected from the group consisting of halo, hydroxy, aryl, C_1-C_6 alkyl substituted aryl, nitro, polycyclic aryl alkyl containing 2 to 4 aromatic rings wherein the alkyl is a C_1-C_6, C_3-C_8 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 hydroxyalkyl, C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl, aryloxy, acyloxy, acyloxy C_1-C_6 alkyl, amino, monoalkylamino wherein the alkyl is C_1-C_6, dialkylamino wherein the alkyl is C_1-C_6, acylamino, ureido, thioureido, carboxy, carboxy C_1-C_6 alkyl, azido, cyano, cyano C_1-C_6 alkyl, formyl, acyl, dialkoxy alkyl wherein the alkoxy and alkyl are independently C_1-C_6, aminoalkyl wherein the alkyl is C_1-C_6, and SO_nR' wherein n=0, 1, 2 or 3, R' is H, a C_1-C_6 alkyl or aryl; or a pharmaceutically acceptable salt thereof.

42-48. (Canceled)

49. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound or a pharmaceutically acceptable salt of claim 5.

50. (New) The pharmaceutical composition of claim 49, further including an antineoplastic alkylating agent.

51. (New) The pharmaceutical composition of claim 49, wherein the pharmaceutically acceptable carrier is polyethylene glycol.

52. (New) The pharmaceutical composition of claim 50, wherein the antineoplastic alkylating agent is a chloroethylating agent.

53. (New) The pharmaceutical composition of claim 50, wherein the antineoplastic alkylating agent is a methylating agent.

54. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound or a pharmaceutically acceptable salt of claim 9.

55. (New) The pharmaceutical composition of claim 54, further including an antineoplastic alkylating agent.

56. (New) The pharmaceutical composition of claim 54, wherein the pharmaceutically acceptable carrier is polyethylene glycol.

57. (New) The pharmaceutical composition of claim 55, wherein the antineoplastic alkylating agent is a chloroethylating agent.

58. (New) The pharmaceutical composition of claim 55, wherein the antineoplastic alkylating agent is a methylating agent.

59. (Withdrawn - new) A method of enhancing the chemotherapeutic treatment of tumor cells in a mammal with an antineoplastic alkylating agent that causes cytotoxic lesions at the O^6 -position of guanine, which method comprises administering to the mammal an effective amount of a compound or a pharmaceutically acceptable salt of claim 5.

60. (Withdrawn - new) A method for treating tumor cells in a mammal comprising administering to the mammal an amount effective to reduce the O^6-alkylguanine-DNA alkyltransferase activity in the mammal of a compound or a pharmaceutically acceptable salt of claim 5 and administering to the mammal an effective amount of an antineoplastic alkylating agent which causes cytotoxic lesions at the O^6-position of guanine.

61. (Withdrawn - new) A method of inhibiting the reaction of O^6 -alkylguanine-DNA-alkyltransferase with an alkylated DNA comprising reacting the O^6 -alkylguanine-DNA-alkyltransferase with the compound of claim 5 or a pharmaceutically acceptable salt thereof.

62. (Withdrawn - new) A method of enhancing the chemotherapeutic treatment of tumor cells in a mammal with an antineoplastic alkylating agent that causes cytotoxic lesions at the O^6 -position of guanine, which method comprises administering to the mammal an effective amount of a compound or a pharmaceutically acceptable salt of claim 9.

63. (Withdrawn - new) A method for treating tumor cells in a mammal comprising administering to the mammal an amount effective to reduce the O^6-alkylguanine-DNA alkyltransferase activity in the mammal of a compound or a pharmaceutically acceptable salt of claim 9 and administering to the mammal an effective amount of an antineoplastic alkylating agent which causes cytotoxic lesions at the O^6-position of guanine.

64. (Withdrawn - new) A method of inhibiting the reaction of O^6 -alkylguanine-DNA-alkyltransferase with an alkylated DNA comprising reacting the O^6 -alkylguanine-DNA-alkyltransferase with the compound of claim 9 or a pharmaceutically acceptable salt thereof.